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July 15th, 2025

Dear Regina,

Welcome to 2025 BioMarketing Insight's monthly newsletter.

Enjoy the recap of my AAPI Heritage Festival and Exhibit celebrations on May 3rd, 6th, 17th and 20th, 2025 with photos.

This month I will be covering "What Is Your Biological Age and How Does the Brain Plays a Role in Aging?". To read more, go to our Table of Content and click on the topic link.

If you missed last month's newsletter on "Score Card: Robert Kennedy Jr. first 100 days at Human Health Services", click on this <u>link</u>.

Please join me on September 15-18 for the BioProcessing International Conference

The next newsletter will be August 15, 2025.

With all the chaos going on due to tariffs that increases consumer prices, elimination of DEI programs that decreased NIH funding, cruel deportations, and reorganization of the HHS have lead to delayed drug/medical device/diagnostic approvals and research. You may need a little inspiration or something to make us laugh to get us through this time of uncertainty, click on the "Inspiration" link to give yourself a few minutes to relax and enjoy the music from the Berklee School of Music in their song "What the World Needs Now," and ending with Celine Dion and Josh Groban with "The Prayer".

We encourage you to share this newsletter with your colleagues by using the social media icons below, or by simply forwarding this newsletter or use the link below. Should you or your colleagues want to join my mailing list, click on "join my email list" link below.



Sincerely,
Regina Au
CEO, New Product Planning/Strategic Planning
BioMarketing Insight







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Developing a Product? Commercializing a Product?

If you are developing a product and have not conducted the business due diligence to determine commercial viability or success, contact <u>me</u> for an appointment. For successful commercial adoption of your product or looking to grow your business, contact <u>me</u> for an appointment.

For more information on our services, click on the links below:

Product Development

Scenario Planning - for more information, email me.

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Recap of AANHPI Heritage Festivals and Exhibit in May

We, AAPIEC Inc. is pleased to announce we celebrated AAPI/AANHPI Heritage Month in two (2) locations this year. In collaboration with Middlesex Community College (MCC) for a 2nd year on May 6, 2025 in Lowell and a new location, Boston Lyric Opera on May 17, 2025 in South Boston.

In addition, we were invited to display our Contributions AAPI Have Made to American History Exhibit, at the Brookline AANHPI Heritage Festival on May 3, 2025 and the Network for Social Justice (NFSJ) AAPI Heritage Festival at Winchester High School on May 20, 2025.

All these events could not be possible without the support of our sponsors. Thank you to our sponsors listed below.

Platinum

Asian Community Fund/The Boston Foundation

Mass Cultural Council

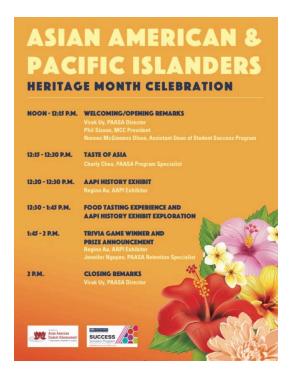
Billerica Cultural Council

Dracut Cultural Council

Chelmsford Cultural Council
Tewksbury Cultural Council

They were all successful in celebrating AAPI Heritage Month and getting the word out as to who AAPIs are and the Contribution every ethnic group contributed to American History. AAPI History is Part of American History.

See the Agendas below for the May 6th and May 17th events and a few pictures of each event. To see a full slide show of photos, visit our <u>website</u>.





At MCC, on May 6th, there was a "Taste of Asia" where various local ethnic restaurants were present for attendees to sample. All restaurants were delicious. In addition, our Contributions AAPI Have Made to American History was on display and a Trivia Contest with prizes were held based on the exhibit information.

At the Boston Lyric Opera venue, we had a full program of performers, speakers, cultural exhibitors and food vendor, MeiMei Dumplings. After all, how can one have an Asian Festival without food. Our Contribution Exhibit was also display and Trivia Questions with prizes were also held. See agenda for speaker and performers, and below for cultural exhibits, restaurant and volunteers.

Cultural Exhibitors:

Asian Indian American - Ekam Boston Nagasree Chakka, Arya Kodumuru, and Sheethal Kundoor
Cambodian American - Kirirath Saing
Chinese American - Chinese Historical Society - Alice Kane
Filipino American - Pamana Inc. - Jelyn Masa and Stacey Domingo
Native Hawaiian - AAPIEC Inc. - Regina Au

Restaurant:

MeiMei Dumplings - Founder, Irene Li

Volunteers:

Emma Trowbridge
Sarah Curtis
Christina Fu
Theodore Chin
Carlo Miguel Bunyi
Alice Kane

Photos from May 6th and May 17th, 2025 AANHPI Heritage Festival and Exhibit





Middlesex Community College (MCC), May 6, 2025

First photo: Charly Chea, PAASA Program Specialist on right and student on left in front of Contributions AAPI Have Made to American History Exhibit.

Second photo: Group shot, with Virak Uy, Director of PAASA, left, MCC President Phil Sisson, third from the left, Regina Au, President of AAPIEC Inc. fourth from the left and students.







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May 17, 2025 AAPI Heritage Festival and Exhibit.

- Photo 1: Indras Artistic Creation welcomes you to the Festival and Exhibit
- Photo 2: Sarah Curtis, vocalist and Emma Trowbridge, pianist,
- Photo 3: The Philippine Dance and Culture Organization,
- Photo 4: Ekam USA three traditional Asian Indian Instruments, and
- Photo 5: Duo Filipino Lauren Florek, soprano and Carlo Miguel Bunyi, baritone with

Marceline Merrill on piano.

For a full slide show of photos, click here.

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informa -



September 15-18, 2025 Hynes Convention Center Boston, USA

Save the Date: September 15-18, 2025 BioProcess International, Boston

I am pleased to announce that I will be a Speaker at the BioProcess International Conference on September 17th, 2025. The title of my presentation is "Creating a Winning Target Product Profile: A Roadmap for Successful Biopharmaceutical Development". For more information on my presentation, click here. For more information on the agenda, other speakers, and to register, click <a href=here.



5th Edition International Vaccines Congress (IVC 2025) Conference on October 23-25, 2025 in Orlando, FL

I am pleased to announce that I will be a Key Note Speaker and a Scientific Committee Member at the IVC 2025 Conference in Orlando, FL, October 23 - 25, 2025. The title of my presentation is "The importance of post-marketing surveillance and real-world data: For a product to be successful". Information on Scientific Committee members, click here. For more information on the conference, click here.



Inspirations

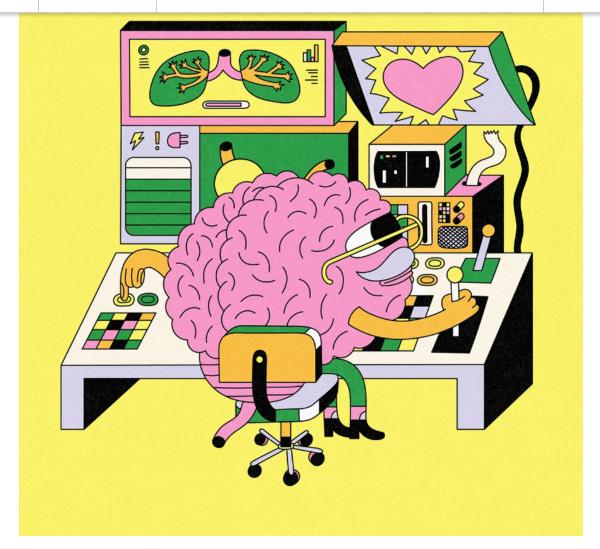
Even with the current uncertainty of our country, we will get through it. Keep voicing your opinion on what is right, what is wrong and the needs of the people. This is the only way things will change.



Let's End with Celine Dion & Josh Groban Singing "The Prayer"

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What Is Your Biological Age and How Does the Brain Plays a Role in Aging?

Credit: Fabio Buonocore

Scientists have been studying the ageing process for at least 50 years. Aging and death are inevitable, but scientists are trying to develop an "Ageing Clock" that could be used early in life to assess an individual's risk of age-related illness, when it might still be possible to intervene. They could also aid in testing treatments aimed at slowing ageing, by providing a marker to track the effects of the intervention in real time. Read on about Ageing Clocks, a New Theory on Aging and Seeking New Treatment.

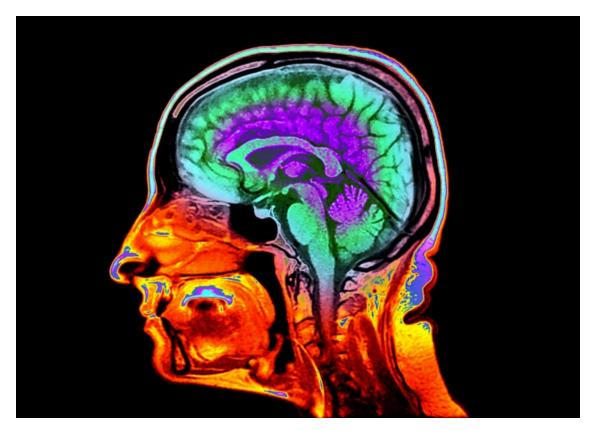
What is an Ageing Clock?

First-generation epigenetic clocks were trained on chronological age, but the more precisely they predicted chronological age, the less they could predict clinical outcomes due to substantial <u>individual variation</u> in the rate of aging; people born in the same year can age slower or faster than their peers.

regarded as a potentially preventable cause of chronic disease.

However, these clocks were developed on cross-sectional phenotypes in multiage samples, not on longitudinal observations of the same person as recommended in geroscience, understanding the biological mechanisms of aging and how these mechanisms contribute to the development of age-related chronic diseases.

This limitation led to the development of a third-generation longitudinal brain imaging approach to measuring aging.



A magnetic resonance imaging scan (pictured, artificially coloured) of the brain can detail the risk of memory loss and other cognitive difficulties.

Credit: Zephyr SPL

To develop an improved clock, <u>Ethan Whitman</u>, who studies brain ageing at Duke University in Durham, North Carolina, and his colleagues began with a remarkable study of more than 1,000 people born in Dunedin, New Zealand, between April 1972 and March 1973, who have been periodically assessed since birth by researchers. In the most recent of those assessments, participants' brains were scanned using magnetic resonance imaging.

Whitman used 860 brain images across two decades (ages = 26, 32, 38 and 45 years) into their algorithm looking for correlations between the brain-scan data which measured 19

the team called the Pace of Ageing.

A <u>new ageing clock</u> was formed: higher scores on the measure were correlated with greater risk of future chronic diseases and death. This was true not only in the Dunedin participants, but also when the researchers used images from 42,583 participants in the UK Biobank and 1,737 brain scans from the Alzheimer's Disease Neuroimaging Initiative.

Currently the most widely used measures for estimating individual differences in aging is Age-sensitive alterations in DNA methylation, referred to as epigenetic clocks.

When <u>Kim Kardashian</u> had her epigenetic profile done through a commercial blood test from TruDiagnostic, she found that her "biological age" was of a 34 year old instead of her chronological age of 43, which was broadcasted on the season finale of *The Kardashians* in July of 2024.

Epigenetic biological clocks that assess your biological profile have gained a lot of traction. In <u>December 2024</u>, the US Advanced Research Projects Agency for Health announced a programme to develop and validate biomarkers of ageing. Hevolution Foundation, a charity in Riyadh, has invested US\$400 million in healthspan research. And organizers of XPRIZE Healthspan — a competition to find treatments for conditions associated with ageing — are planning a 7-year, \$101-million global competition that is dedicated to improving healthspan.

Several tests to assess ageing already exists. Geneticist <u>Steve Horvath</u>, now at Altos Labs in Cambridge, UK, developed one of the <u>first epigenetic clocks</u> more than a decade ago. He analyzed 800 samples to catalogue which sites in the genome were tagged with methyl groups — a chemical modification to DNA that helps to regulate the expression of genes. Applying a machine-learning algorithm, the algorithm identified 353 methylation sites that, taken together, correlated with participants' chronological ages. Some of these sites were more methylated with age; others were less so.

Those markers became the basis for a test that can predict a person's chronological age with remarkable accuracy. But the test was not as good at predicting how long a person might expect to remain healthy, or when they might die.

Horvath's team developed new tests to search for methylation sites that correlate with other age- and health-related measures, such as white-blood-cell counts, the amount of glucose in the blood and levels of a protein that serves as a marker for inflammation. This time, the goal was to create a clock that reflected a person's time to death, rather than merely the number of years lived.

associated with factors such as cigarette smoking or the risk of heart disease, among other ailments.

Seeking Validation

The hype surrounding ageing research has also created a false impression of how well tested the markers have been in different populations, or in different settings, says <u>Mahdi Moqri</u>, a computational biologist at Harvard Medical School in Boston, Massachusetts. Although epigenetic-clock markers have been used in a vast range of studies, they typically have not been sufficiently validated for use as primary outcomes in clinical trials, he says. "Even those who are running clinical trials, they think that these biomarkers are more advanced than they actually are," said Mogri.

There is also disagreement about what the clocks really measure. In a survey of more than 100 participants at a scientific conference on ageing research, about 30% defined ageing as the loss of function that comes with time. Other definitions included the accumulation of damage with time; a developmental stage; and an increase in disability and death. "Defining biological age is a whole touchy subject in itself," says Marije Sluiskes, a biostatistician at Leiden University Medical Center.

Reliability of the tests has also been a concern. A <u>2022 study</u> found that six epigenetic clocks frequently used by researchers can yield variable results, with some varying by up to nine years even when the same samples were used.

Another study published in 2024 analyzed changes in a whole host of measures, including metabolites, proteins and microbes in 108 people aged 25–75. The researchers found that molecular markers of ageing changed in a nonlinear way, with bursts of change when people reached their mid-forties and when they hit 60 which some call "periods of accelerated ageing" with no concrete theory as to why this happens.

Brian Chen, a molecular epidemiologist at California Pacific Medical Center Research Institute in San Francisco thinks these tests need more work because there is a lot of confusion on how to interpret the results and validating them. "I've seen, in academia, scientists trying to promote and hype up 'biological age' and ageing research in general to generate more interest and funding." Chen decided to go back to the basics in understanding the biology of ageing, with the goal of building new markers from there. "Let's focus on the mechanism first, so that we know why it might cause ageing," he says. "I'm just trying to follow the breadcrumbs."

A New Theory on Aging

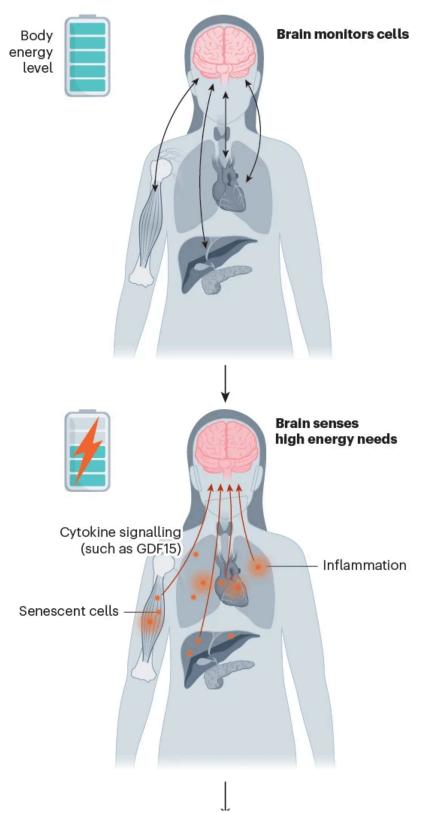
A biology paradox? As humans grow older, their metabolisms tend to slow, they lose muscle mass, and they burn many fewer calories. But certain cells in older people appear

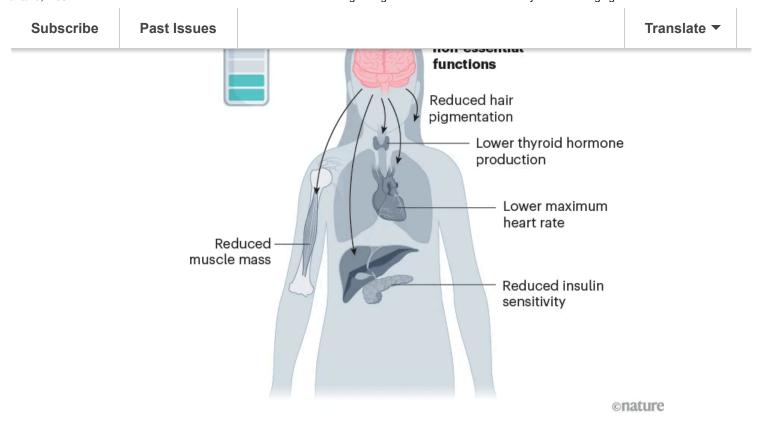
These energy consumers are called senescent cells. They are older cells that have stopped dividing and no longer perform the essential functions that they used to. Because they seem idle, biologists have coined them zombie-like senescent cells assuming they use less energy than when they were young, says Martin Picard, a psychobiologist at Columbia University in New York City.

But in 2022, Gabriel Sturm, a former graduate student of Picard's, found that cells that had stopped dividing had a metabolic rate about double that of younger cells.

For Picard and his colleagues, the energetic mismatch wasn't a paradox at all: ageing cells accumulate energetically causing costly damage, such as alterations in DNA, they initiate pro-inflammatory signalling, and the <u>shortening of telomeres</u> — the stretches of <u>repetitive DNA</u> that cap the ends of chromosomes and protect them.. How that corresponds with the relatively low energy expenditure for ageing organisms is still unclear, but researchers hypothesize that this over consumption for energy might be an important driver of many of the negative effects of growing old, and the brain who acts like a mediator or brain—body energy conservation (BEC) model of aging. As some cells get older and require more energy, the brain reacts by stripping resources from other biological processes, ultimately resulting in outward signs of ageing, such as greying hair or a reduction in muscle mass (see 'Energy management and ageing' Image 1).

the body. As cells age and damage to them accumulates, some will enter a state of senescence. They stop dividing and start eliciting energetically costly processes, such as inflammation. They secrete signalling molecules called cytokines, including GDF15, which indicate elevated energy demands to the brain. The brain, sensing this hypermetabolic state, compensates by suppressing energy usage in other parts of the body, resulting in some of the signs of ageing, such as greying hair, reduced maximum heart rate and a reduction in thyroid hormone.





Energy Management and Ageing, Image 1

Some researchers say this concept of the 'brain–body energy-conservation model' (BEC), could shed light on how psychological stress can accelerate ageing at a molecular level. Once dismissed as being on the fringes of ageing research, this idea is now becoming mainstream, says <u>Alessandro Bartolomucci</u>, a biologist at the University of Minnesota in Minneapolis. "The science speaks for itself. The field cannot dismiss it."

to poor health in pointing to the brain's role in ageing, says Elissa Epel, a health psychologist at University of California, San Francisco (UCSF). "But we didn't know as much about what was happening at the cellular level."

They decided to look at telomere length. Telomeres progressively shorten over the lifespan of an organism, and this process has been linked to senescence and other forms of agerelated changes in cells.

Epel and her team recruited mothers who had healthy children and mothers who had a child with a chronic illness. They found that the women with a chronically ill child had shorter telomeres than those who did not — and that telomere length correlated with the number of years spent as a carer. These findings suggested that exposure to chronic stress can introduce molecular changes that are important for ageing, says biologist Noah Snyder-Mackler at Arizona State University in Tempe.

Since then, evidence of telomere shortening in people exposed to other stressors, such as adverse experiences in childhood and work-related exhaustion have been found. While some of the results have been mixed regarding telomere length, there has been other evidence linking stress to other molecular markers of ageing.

Picard and his colleagues think that their BEC model could provide a framework for thinking about how the effects of stress could be transmitted from brain to body. Their team have focused on one molecule thought to be an important player in human ageing: growth differentiation factor 15 (GDF15), a cytokine, or cellular messenger.

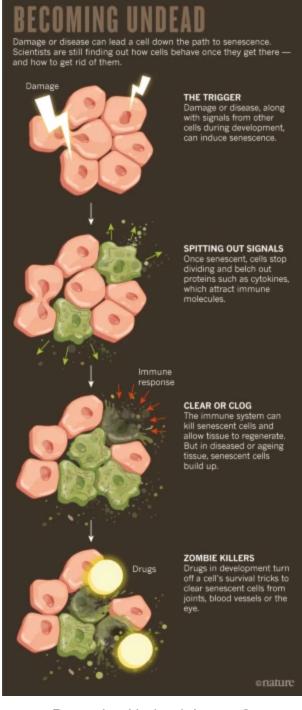
It has been linked to ageing-related processes, including cellular senescence and the dysfunction of mitochondria, which are the powerhouses of cells, as well as age-related diseases, such as Alzheimer's disease. It is elevated in various chronic physical and mental illnesses, and cause nausea and appetite loss associated with pregnancy, cancer and other conditions. Although GDF15 is secreted by many organs, its receptor is **only** found on the brain. These characteristics suggest that GDF15 is responsible for sending the brain signals about cellular stress.

Many questions remain to be answered. One important avenue of future research will be teasing apart the effects of the type and timing of stressors on the trajectory of ageing — and how and when the different age-related biological changes overlap. "We always want a simple answer. We want one measure of ageing, like the epigenetic clock or telomeres," Epel says. "But biology is not that simple."

Seeking New Treatments?

Jan van Deursen and his colleagues at Mayo Clinic in Rochester, Minnesota, had an idea: could killing off these 'zombie' cells in the mice delay their premature descent into old age?

In a 2011 study, the team found that eliminating these <u>'senescent' cells</u> prevented many of the ravages of age. This set off a flurry of studies where dozens of experiments have confirmed that senescent cells accumulate in ageing organs, and that eliminating them can alleviate, or even prevent, certain illnesses (see 'Becoming undead' Image 2). A <u>2017 study</u> demonstrated that clearing the cells in mice has been shown to restore fitness, fur density and kidney function. It has also improved <u>lung disease</u> and even mended damaged <u>cartilage</u>. And in a 2016 study, it seemed to extend the lifespan of normally ageing mice.



Becoming Undead, Image 2

Hopkins University in Baltimore, Maryland. It jump-starts some of the tissue's natural repair mechanisms, she says.

Now biotechnology and pharmaceutical companies are anxious to test drugs known as senolytics — that kill senescent cells in the hope of rolling back, or at least forestalling, the ravages of age. Jan van Deursen, one of the co-founder of Unity Biotechnology in San Francisco, California, is developing the <u>first senolytic therapy</u> for the treatment of retinal diseases now in Phase 1 & 2. UBX1325 is a potent small molecule that targets BCL-xL, a protein that senescent cells rely on for survival.

At Mayo, gerontologist James Kirkland, who took part in the 2011 study, has cautiously done a handful of small, proof-of-concept open label trial using senolytics in patients with idiopathic pulmonary fibrosis (IPF). It's associated with accumulation of senescent cells in the lungs and quite a bit of frailty. When a short term of senolytic is used, frailty could be alleviated. Dr. Kirkland is also looking at obesity which is associated with incredible senescent cell accumulation and with early onset of age-related diseases. "I lose sleep at night because these things always look good in mice or rats, but when you get to people you hit a brick wall," says Kirkland.

If there is "a whiff of human efficacy", says Unity's president and co-founder, Nathaniel (Ned) David, there will be a massive push to develop treatments and to better understand the fundamental process of ageing. Researchers are watching closely. Senolytics are "absolutely ready" for clinical trials, says Nir Barzilai, director of the Institute for Aging Research at the Albert Einstein College of Medicine in New York City. "I think senolytics are drugs that could come soon and be effective in the elderly now, even in the next few years."



Closing Thoughts

I completely agree with Elissa Epel, health psychologist at UCSF who advised that with these Epigentic clocks or new theories on ageing, one important avenue of future research will be teasing apart the effects of the type and timing of stressors on the trajectory of ageing — and how and when the different age-related biological changes overlap. "We always want a simple answer. We want one measure of ageing, like the epigenetic clock or telomeres, But biology is not that simple." said Epel.

Biology is very complex and research is slow where any major discoveries or breakthroughs have taken at least 25 or 50 years of research. Sometimes scientist gets so excited about new discoveries, they want to rush to the finish line and sometimes may overlook major factors or interpret key findings as positive to get there.

I also completely agree with Brian Chen, molecular epidemiologist at California Pacific Medical Center Research Institute in San Francisco who decided to go back to the basics in understanding the biology of ageing, with the goal of building new markers from there. "Let's focus on the mechanism first, so that we know why it might cause ageing," he says. "I'm just trying to follow the breadcrumbs." If one doesn't understand the foundation or mechanism of a disease, how can one build upon it with accuracy.

This is an exciting time for this field where a number of potential links have materialized and now it is time to carefully put the pieces of the puzzle together. Validation is one key to success and now, only time will tell.

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